

**R E M A R K S**

Editorial revisions were made to page 4, the paragraph bridging pages 19-20, page 22, and the paragraph bridging pages 26-27 of the specification to correct minor clerical errors in some of the cited publications.

The specification was objected to for the reasons set forth in the first paragraph on page 2 of the enclosed Office Action. The Examiner raised certain informalities with respect to the discussion in the specification of some of the drawings.

Pages 20, 22 and 23 of the specification were amended hereinabove to avoid the objection.

Withdrawal of the objection to the specification is therefore respectfully requested..

A REQUEST FOR INITIALED COPIES OF FORMS PTO-1449, PTO/SB/08A and PTO/SB/08B was mailed to the USPTO on November 24, 2003. Applicants reiterate their request for initialed copies of the FORM PTO-1449 dated May 10, 2001, the Forms PTO/SB/08A and PTO/SB/08B dated August 22, 2001 and the Form PO/SB/08A dated February 12, 2002.

The presently claimed invention concerns a method for the evaluation of the ultrastructure of connective tissue comprising:

(a) providing a fiber optic probe operative in the mid-infrared or near-infrared region of the electromagnetic spectrum,

(b) positioning the probe to be in contact with the surface of the connective tissue for detecting attenuated total reflectance or within a sufficient distance from the surface of the connective tissue for detecting reflection,

(c) detecting mid-infrared radiation or near-infrared radiation penetrating the surface of the connective tissue for detecting attenuated total reflectance or reflecting off of the surface of the connective tissue for detecting reflection, and

(d) analyzing the infrared radiation from step (c) for at least one of peak height, peak area and frequency and comparing at least one of the peak height, the peak area and the frequency established values for at least one of peak height, peak area and frequency for normal connective tissues to detect a modification in the molecular structure of the connective tissue.

Claims 1 to 20 were rejected under 35 USC 103 as being unpatentable over Zakim et al. USP 5,733,739 in view of Hein et al. USP 5,986,770 and Guzelsu et al. USP 6,324,419 for the reasons bridging pages 2 and 3 of the Office Action.

It was admitted in the Office Action that Zakim et al. fail to specifically disclose the use of a fiber optic probe and evaluation of connective tissue.

It was stated in the Office Action that "Zakim et al disclose using either infrared reflectance spectroscopy or infrared attenuated total reflectance techniques for evaluating tissue". However, Zakim et al. do not specify any specific tissue. Furthermore, Zakim et al. do not disclose connective tissue as recited in applicants' claims, such as cartilage, ligament, tendon, capsule and bone. All the claims in Zakim et al. are directed to cells, not tissues.

The gist of Zakim et al. is to detect cancerous cells. Zakim et al. thus discuss PAP smear tests and dysplasia.

Cells and connective tissue are two very different materials and, hence, are studied very differently. Cells are spheroidal, 8 to 25 microns in size, and can grow outside the body. Cells also have specific components within them, such as DNA, that are not present in "tissue" and, specifically, not connective tissue. Conversely, the presently claimed invention is directed to studying connective tissue, the semi-solid material that comprises the bulk of the body. Thus cells and connective tissues are distinct entities.

Zakim et al. evaluate cells for pre-cancerous and cancerous changes, alterations that cannot be identified in connective tissue. In the presently claimed invention, changes in cells are not being evaluated but, rather, molecular changes in connective tissue components that arise from catabolism abnormalities (destructive metabolism) are being evaluated. This has nothing to do with malignancy.

In summary, Zakim et al. do not teach or disclose a method to detect a modification in the molecular structure of connective tissue.

Neither Guzelsu et al. nor Hein et al. disclose utilizing infrared radiation to evaluate molecular changes. In both Guzelsu et al. and Hein et al., a light source is utilized, but it is used such that it interacts with tissue, is reflected back, and the "amount" of light reflected back correlates with a bulk tissue property. There is no information in either Guzelsu et al. or Hein et al. concerning the molecular composition of the tissue being examined. With spectroscopy, the technique used in the presently claimed invention, individual frequencies are examined and related to molecular structure. As discussed above, it is specifically recited in applicants' claim 1 "to detect a modification in the molecular structure of the connective

tissue".

In Guzelsu et al, the amount of light correlates with the amount of "stretch" in a connective tissue (skin). As discussed above, in Hein et al., no molecular information is provided. Hein et al. essentially characterize a sample by shining light on it, and measuring how the light is scattered back. This can provide information on some "macroscopic" structures of a sample, but certainly no information on individual molecules.

Therefore, the statement at the middle of page 3 of the Office Action that "Such a modification [of Zakim et al., by utilizing a probe such as that described in Hein et al. or Guzelsu et al.] merely involves the substitution of one known type of probe having a light source for another" is not correct. Again, spectroscopy, (studying different frequencies of light or radiation as related to molecular interactions) is substantially different from just looking at the quantity of light (radiation).

The following is stated in the Office Action: "Hein et al. disclose infrared spectroscopic evaluation of connective tissue (column 8, lines 11 to 24)." This statement is incorrect, since Hein et al. nowhere mention infrared spectroscopic evaluation.

Furthermore, none of the cited references mention cartilage, such as in the applicants' claims 6 and 8, which recite the following:

"6. The method of claim 1, wherein the connective tissue is selected from the group consisting of articular cartilage, meniscal cartilage, ligament, tendon, capsule and bone.

8. The method of claim 1, wherein the connective tissue is cartilage."

In summary, Hein et al and Guzelsu et al. do not refer to the same "type" of analysis that is carried out in applicants' claims. Applicants' presently claimed invention employs infrared spectroscopy to analyze molecules in tissue, not to analyze bulk tissue. An infrared spectrum gives information for the molecules in the tissue, not for a bulk tissue property, or even for the macroscopic structure of the tissue. The peak shifts (frequency changes) recited in applicants' claims are related to molecular vibrations. It is a well-known and extremely well-documented fact in the scientific literature that spectroscopy is a separate field from light scattering or the quantitation of reflective light.

It is respectfully submitted that one of ordinary skill in the art would not arrive at the presently claimed invention from the cited references because (i) Zakim et al. do not concern connective tissue and do not teach or suggest detecting a modification in the molecular structure of connective tissue and (ii) Guzelsu et al. and Hein et al. do not teach or suggest using infrared radiation to evaluate molecular changes in connective tissue.

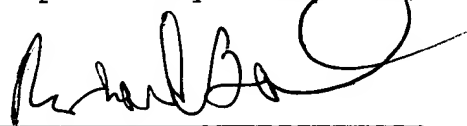
It is therefore respectfully submitted that applicants' claimed invention is not rendered obvious over the references, either singly or combined in the manner relied on in the Office Action, in view of the many distinctions discussed hereinabove. It is furthermore submitted that there are no teachings in the references to combine them in the manner relied on in the Office Action.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

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Respectfully submitted,



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